REMARKS

Claims 4 and 6-8 currently appear in this application. The Office Action of May 12 and the Advisory Action of August 22, 2008, have been carefully studied. These claims define novel and unobvious subject matter under Sections 102 and 103 of 35 U.S.C., and therefore should be allowed. Applicant respectfully requests favorable reconsideration, entry of the present amendment, and formal allowance of the claims.

Amendment

Claim 4 has been amended to recite that the nucleic acid probe is a DNA fragment of a chemically synthesized DNA comprising a nucleic acid sequence complementary to the target nucleic acid. Support for this amendment can be found in the specification as filed at page 4, lines 15 and 16l page 18, line 16 and page 19, last paragraph.

Art Rejections

Claims 4, 6 and 7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Larsson et al., (1994) C. Am. Chem. Soc. 116:8459-8465 further in view of Juarranz et al., (1996) *J. of Microscopy* **182** Pt 1, 46-49.

This rejection is respectfully traversed. At page 5, line 3 to the bottom line, the Examiner has compared the method claimed in claim 4 to the disclosure of Larsson et al., and states that "a nucleic acid probe" of the

presently claimed method corresponds to "YOYO" in Larsson. However, it is respectfully submitted that this is not correct. The technical feature of "a nucleic acid probe" of claim 4 does not correspond to "YOYO" of Larsson.

Claim 4 is drawn to a method for detecting a hybrid nucleic acid using a cationic dye compound. This method comprises the following four steps:

(i) providing a specific cationic dye compound;

(ii) contacting a nucleic acid probe with a sample containing a target nucleic acid to form a hybrid nucleic acid, wherein t that the nucleic acid probe is a DNA fragment of a chemically synthesized DNA comprising a nucleic acid sequence complementary to the target nucleic acid

(iii) binding the cationic dye compound to the hybrid nucleic acid; and

(iv) measuring the circular dichroism (CD) of the cationic dye compound bound to the hybrid nucleic acid.

Submitted herewith is a figure illustrating the procedure claimed in claim4.

$$X\text{-}(Y\text{-}Z)_n \quad (I)$$

It should be noted that the nucleic acid probe used in step (ii) of the method claimed herein is not the same as the "cationic dye compound" used in step (iii). The specification as filed states that the nucleic acid probe used in step (ii) includes, but is not limited to, DNA fragments and chemically synthesized DNA (see page 19, last paragraph), and it is clear that the nucleic acid probe used in step (ii) of the herein claimed method is different from the cationic dye compound used in step (iii). Claim 4 has been amended to make it clear that the nucleic acid probe in the herein claimed process is not the same as the Larsson YOYO.

From a correct reading of the claimed method, it is readily apparent that step (ii) as amended does not exist in the method of Larsson. Specifically, Larsson uses double-stranded (ds) DNAs such as "linear coliphage T2 DNA (164kbp)" and "circular PhiX 174 RFI DNA (5386 bp)", as described at page 8459, right column, second line from the bottom of page 8460. It should also be noted that the method claimed herein makes it possible to detect a specific sequence in the target nucleic acid. On the other hand, Larsson does not use a probe such as a DNA fragment, and it is not possible to detect a specific sequence in a target nucleic acid.

Juarranz adds nothing to Larsson, because Juarranz uses the human HeLa epithelial carcinoma cell line, and does not conduct a hybridization step of a nucleic acid with a DNA probe as in step (ii) of the presently claimed method.

As described on the last page, left column, lines 23-25 of Juarranz, the method disclosed relates to *in situ* measurement.

Accordingly, even if one skilled in the art were to combine Larsson and Juarranz, this combination would not include a hybridization step corresponding to step (ii) of the presently claimed method. Thus, a combination of Larsson and Juarranz does not result in the method claimed herein. Therefore, it is respectfully submitted that the presently claimed method is not obvious over a combination of Larsson and Juarranz.

In addition, the presently claimed method has definite advantages over the methods in either Larsson or Juarranz. The method claimed herein achieves a remarkable effect so that hybrid nucleic acid can be stably and accurately detected using measurement of the CD spectrum. On the other hand, the method of Larsson would presumably not make it possible to measure DNA accurately because the cationic dye used in Larsson intercalates into the DNA and stabilizes the structure of the cationic dye/DNA complex, which impairs stable and accurate detection of the DNA.

The herein claimed method includes step (ii), namely, using a nucleic acid probe wherein that the nucleic acid probe is a DNA fragment of a chemically synthesized DNA comprising a nucleic acid sequence complementary to the target nucleic acid. Therefore, this method makes it possible to specifically detect a target nucleic acid-containing sequence.

The method claimed herein uses a cationic dye compound, which makes it possible to detect a target nucleic acid with high accuracy, which is not the case with the Larsson method. The dye used in Larsson, such as YOYO, intercalates into a ds DNA, and this intercalation impairs the structural stability of the dye compound/nucleic acid complex, which results in unstable and inaccurate CD detection of the hybrid nucleic acid. This is supported by Larsson in the Abstract, lines 5-6, "This conclusion is supported by the induced negative circular dichroism (CD), the transfer of energy from the DNA bases into the bound YOYO **and the unwinding of supercoiled DNA by YOYO**." [emphasis added]

In contrast thereto, the present specification at page 14, lines 6-9, specifically states, "Such an intercalation between base pairs will be a factor impeding the detection of the circular diachronic of the chromophore X."

The presently claimed method uses a cationic dye as defined in claim 4, which makes it possible to detect a target nucleic acid using a small amount of the dye. This is not the case in Larsson, because the dye used in Larsson, such as YOYO, intercalates into a ds DNA, and then binds with DNA in an external binding mode (see abstract). Therefore, to measure a CD spectrum for detecting a target nucleic acid, a high amount of YOYO, that is, an amount sufficient for filing the intercalation site as well as binding with the target nucleic acid in an external binding mode must be used.

Accordingly, in view of the above-described advantages of the present invention, it is respectfully submitted that the herein claimed method is not obvious over the cited references.

Respectfully submitted,

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